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RESEARCH ARTICLE



Cost of agronomic biofortification of wheat with zinc in China

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Abstract Biofortification is a strategy for overcoming human zinc (Zn) deficiency, especially in rural areas of developing countries. Actually, biofortification by foliar Zn application has been demonstrated at small scale, but not at large scale due to the absence of economic analysis. Therefore, here, we conducted the first cost-effectiveness analysis using the method of "disability-adjusted life year" measuring the health burden. We thus quantified the cost of agronomic biofortification of wheat with Zn in three major wheat-growing regions of China. Our results show that the current annual health burden due to human Zn deficiency, defined as numbers of disabilityadjusted life years lost, is 0.21 million years for the region under single wheat plantation, 0.79 million years for the region under wheat-maize rotation, and 0.38 million years for the region under wheat-rice rotation. Comparing with traditional wheat diets in these three regions, the consumption of agronomically Zn-biofortified wheat diets could increase the daily Zn intakes of infants and children under 5 years of age. These increased daily Zn intakes consequently reduce the

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health burden due to human Zn deficiency in these regions by up to 56.6 %. According to cost-effectiveness analysis, the cost for saving one disability-adjusted life year in these regions ranges from US\$ 226 to US\$ 594 for foliar Zn application alone. The cost ranges from US\$ 41 to US\$ 108 when foliar Zn and pesticide applications are combined to reduce labor costs. This cost of US\$ 41–108 under the combined application of foliar Zn plus pesticide is lower than the World Bank's standard.

Keywords Cost-effectiveness analysis · Disability-adjusted life year · Foliar zinc application · Pesticide · *Triticum aestivum*

1 Introduction

Zinc (Zn) plays numerous essential roles in biological systems and has been paid ever-increasing attention because of the widespread deficiency of Zn in soils, crops, and human beings around the world (Hotz and Brown 2004; Alloway 2008). Zinc deficiency affects about 2 billon human beings, most of whom are pregnant women and children under 5 years of age (WHO 2012). The "disability-adjusted life year" is a health measurement that describes both mortality and morbidity of a health condition as a single index. For instance, human Zn deficiency in 2004 resulted in 3.8 % of "disability-adjusted life-years" in children under 5 years of age (Black et al. 2008). Biofortification, an upcoming strategy for developing micronutrient-enriched staple food crops to alleviate human micronutrient deficiencies, has been increasingly considered along with traditional strategies such as medical supplementation, food fortification, and dietary diversification during the last two decades (Welch and Graham 2004; Cakmak 2008; Bouis et al. 2011; Solymosi and Bertrand 2012). Because of the close connection of Zn flow among the soil-crop-human



continuum (Welch 2008), Zn-biofortified staple food obtained by using either genetic (breeding) or agronomic strategies can be daily consumed by resource-poor rural residents to increase their Zn nutrition and health status (Fig. 1).

Wheat (Triticum aestivum L.) is one of the most important staple crops around the world. However, more than half of wheat plantation is in Zn-deficient soils and the Zn concentration in wheat grain is generally too low to supply sufficient Zn nutrition for human health (Alloway 2008; Cakmak 2008). Therefore, more attention has been paid to the improvement of human Zn intake by biofortification of wheat grain with Zn (Schroeder et al. 2013; Wheeler and von Braun 2013; Myers et al. 2014; Wani et al. 2015). The genetic biofortification via breeding Zn-enriched wheat varieties represents a long-term strategy with important advantages. For example, it can be extended to the malnourished rural areas, and it is sustainable because of its low recurrent expenditures (Khoshgoftarmanesh et al. 2010; Bouis et al. 2011). The genetic biofortification is also expected to have a low cost and high cost-effectiveness according to ex-ante assessments (Stein et al. 2007; Ma et al. 2008; Meenakshi et al. 2010; De Steur et al. 2012). Although field trials with both local varieties and Zn-biofortified varieties are still under way (Bouis et al. 2011; Velu et al. 2012), the breeding strategy has limitations. For example, these Znbiofortified varieties could perform poorly because of adverse soil conditions such as low available Zn, high pH, drought, phosphorus buildup, and unbalanced metal concentrations (Cakmak 2008; Solymosi and Bertrand 2012); yield tradeoff (Zhao et al. 2009); and genetic and environmental interactions (Velu et al. 2012). These limitations or problems cannot be solved in the short term. Alternatively, the agronomic biofortification via Zn fertilization especially by foliar Zn application is increasingly recognized as an effective, complementary, and ready-to-use strategy for biofortifying wheat with Zn (Cakmak 2008). Studies have shown that foliar Zn application can increase and even double grain Zn concentrations of different wheat cultivars in different ecological zones and countries (Zhang et al. 2012; Zou et al. 2012; Velu et al. 2014). The agronomic biofortification of wheat with Zn, however, is often assumed to be costly because it requires repeated annual applications and additional associated expenses (Velu et al. 2014). As a result, the agronomic biofortification of wheat with Zn has not been widely adopted even though the true cost of such biofortification is unknown, i.e., a comprehensive costeffectiveness analysis in wheat-dominated regions has not been conducted (Joy et al. 2015). In contrast, to the labor cost, several recent studies have indicated that labor costs generated by the agronomic biofortification of wheat with Zn could be substantially reduced by including Zn fertilizer in the routine spraying of foliar pesticide (Ram et al. 2015, 2016; Wang et al. 2015; Fig. 1).

China is the biggest producer and consumer of wheat products worldwide, and 100 million Chinese, mostly in rural

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areas, suffer from Zn deficiency (Ma et al. 2008). Meanwhile, China has been listed as the top three prioritized countries in country-level biofortification of wheat with Zn (Asare-Marfo et al. 2013). Thus, there is an urgent need in China and in other countries to enhance the Zn concentration in wheat products and to thereby overcome the Zn deficiency in human nutrition. By applying the widely used "disabilityadjusted life year" method (Stein et al. 2007; Ma et al. 2008; Meenakshi et al. 2010; De Steur et al. 2012), the current study provides a clear cost-effectiveness analysis of the agronomic biofortification of wheat via foliar Zn application. Although the study used data from China, the results should be relevant for other developing countries where wheat is a major crop and where Zn deficiency is a major human health problem.

2 Materials and methods

2.1 Major wheat cropping systems in China

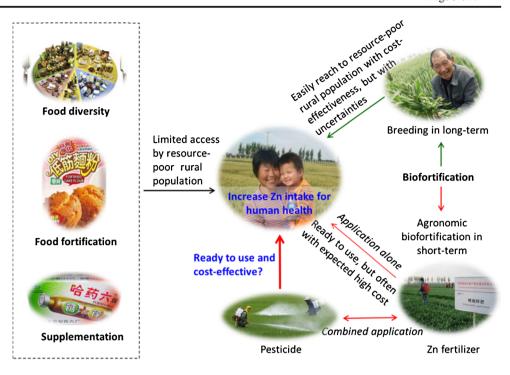
The geographic distribution of the three major wheat cropping systems in central and northern China is shown in Fig. 2. These systems, cross from high to low latitudes, include a single wheat plantation in semiarid/arid area (S-W), a wheat-maize rotation (W-M), and a wheat-rice rotation (W-R), respectively. These three wheat cropping systems occupy about 2.1, 11.7, and 4.6 million hectares and account for 10, 65, and 20 % of the total wheat production in China, respectively (National Bureau of Statistics of China 2013). Nevertheless, the dependency on wheat as a staple food differs among these three regions. Based on the China Health and Nutrition Survey (Jin 2005), the daily consumption of wheat is 90.8, 82.7, and 13.7 g for infants and 181.6, 165.4, and 27.4 g for children under 5 years of age in the S-W, W-M, and W-R regions, respectively.

2.2 Regional economic analysis of agronomic biofortification of wheat with Zn in China

The "disability-adjusted life year" framework, which is commonly used by the World Bank, the WHO, and the HarvestPlus program (Stein et al. 2005), was used to estimate the health burden of Zn malnutrition and the cost-effectiveness of agronomic biofortification of wheat with Zn in the S-W, W-M, and W-R regions in China. The parameters, including daily Zn intake, flour Zn retention, health impact, initial grain Zn, etc. (see Table 1), for estimating the health burden of Zn malnutrition, were adopted from a recent study in China (De Steur et al. 2012). For the subnational socio-economic analysis, the background information of these three wheat cropping regions in China was, respectively, provided as follows. Infants numbered about 1.0, 3.8, and 1.8 million, and children (1 to 5 years old) numbered 4.2, 15.3, and 7.4 million in the S-W, W-M, and W-R

Fig. 1 Strategies to overcome human Zn deficiency in wheatdominated rural regions of China and other countries

China



regions, respectively (National Bureau of Statistics of China 2010). The current health burdens (in term of the numbers of "disability-adjusted life years" lost) due to human Zn deficiency in these regions were calculated with data both from previous studies (Stein et al. 2005; De Steur et al. 2012) and from the ratio of the population in the studied regions to the whole national population. Thus, the current burdens due to Zn deficiency were 55, 202, and 94 thousand "disability-adjusted life years" lost for

infants, and 158, 583, and 281 thousand "disability-adjusted life years" lost for children in the S-W, W-M, and W-R regions of China, respectively.

The information listed in Table 1 was essential for analysis of the health impact of agronomic biofortification of wheat with Zn. With these data, we then calculated the health impact (the numbers of "disability-adjusted life years" saved) of the agronomic biofortification of wheat with Zn by both the handbook

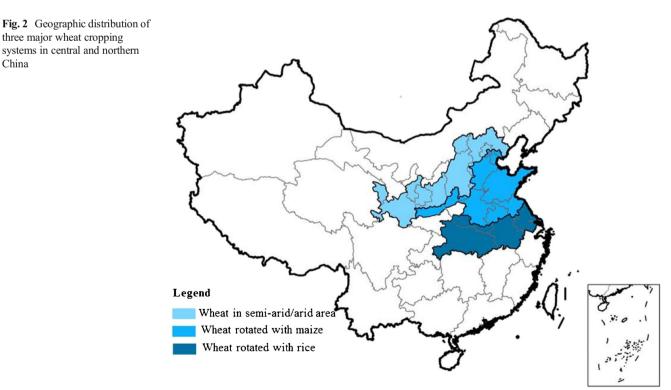




Table 1Health impact of
agronomic biofortification of
wheat with Zn in three major
wheat cropping systems in China

Parameters	Pessimisti	c scenario		Optimistic scenario			
	S-W	S-W W-M W-R		S-W	W-M	W-R	
Scenarios under agronomic biofor	rtification of	wheat with Z	Zn				
Initial grain Zn content $(\mu g g^{-1})^a$	18.6	27.0	25.9	27.4	27.4	27.4	
Improved grain Zn content $(\mu g g^{-1})^b$	30.7	36.3	36.9	48.0	48.0	48.0	
Grain Zn retention during milling (%) ^c	60.0	60.0	60.0	60.0	60.0	60.0	
Flour Zn retention after processing and cooking (%) ^d	90.0	90.0	90.0	90.0	90.0	90.0	
Added micronutrient content (µg per g wheat)	12.1	9.3	11.0	20.6	20.6	20.6	
Coverage rate (%) ^e	20.0	20.0	20.0	60.0	60.0	60.0	
Health impact by agronomic biof	ortification of	f wheat with	Zn				
Daily Zn intake (mg per day, st	tatus quo) ^f						
1. Infants	4.9	4.9	4.9	4.9	4.9	4.9	
2. Children	6.0	6.0	6.0	6.0	6.0	6.0	
Daily Zn intake with agronomi	cal biofortifie	ed wheat (mg	g per day)				
1. Infants	5.5	5.3	5.2	5.9	5.8	5.3	
2. Children	7.2	6.8	6.5	8.0	7.8	6.7	
% of recommended nutrition in	ntake with ag	ronomical bi	ofortified wł	neat ^g			
1. Infants	79.6	77.0	75.0	85.7	84.3	76.2	
2. Children	89.8	85.4	81.8	100.0	98.0	83.9	
Health impact ("disability-adju	sted life year	s" saved)					
1. Infants	5927	16,354	5452	25,773	89,778	20,654	
2. Children	22,063	79,975	28,100	94,849	348,209	103,308	
3. Total (infants and children)	27,990	96,329	33,552	120,622	437,987	123,962	
4. % of current health burden	13.1	12.3	8.9	56.6	55.7	32.8	

S-W single wheat plantation, W-M wheat-maize rotation, W-R wheat-rice rotation

^{a,b} Initial and improved grain Zn content under the pessimistic scenario was based on field studies in China (Zhang 2012), while grain Zn content under the optimistic scenario was based on field studies in multiple countries (Zou et al. 2012) ^c Based on 85 % flour yield (Tang et al. 2008)

Dased on 85 % nour yield (Tang et al

^d Based on Bouis et al. (2011)

^e Based on and updated from genetic biofortification studies (Stein et al. 2005; Stein et al. 2007; De Steur et al. 2012). Here, the basic assumption of coverage rate is that all consumers replace a certain percentage (20 or 60 %) of their consumption with the biofortified wheat and continue to consume some unfortified wheat in parallel, because biofortified and non-biofortificated wheat cannot be distinguished based on appearance (Stein et al. 2005)

^fBased on the China National Nutrition and Health Survey 2002 (Chai 2009)

^g Based on the WHO recommended nutrition intake levels for Zn in developing countries (Allen et al. 2006)

of "disability-adjusted life year" method (Stein et al. 2005) and a related method used in a study in China (De Steur et al. 2012). To simplify the scientific terminology, we also present the health impact of the agronomic biofortification as a percentage of the current health burden.

Because agronomic biofortification of current wheat varieties by foliar Zn application is a ready-to-use technology (Cakmak 2008), its cost will be different from that of the genetic biofortification (Stein et al. 2005; Qaim et al. 2007; Bouis et al. 2011). Therefore, items contributing to the cost of fined. Based on our field studies and rural surveys (Zhang et al. 2012; Zou et al. 2012; Wang et al. 2015) and on the recent prices of commodities in China, we estimated the costs of agronomic biofortification (Table 2). The costs include Zn fertilizer, agricultural equipment (motorized sprayer and water tank), and labor and extension services, but do not include social marketing when the foliar Zn application was conducted alone. In most practical situations, the combined foliar application of Zn fertilizer plus pesticide is employed (Ram

agronomic biofortification of wheat with Zn should be de-



et al. 2015, 2016; Wang et al. 2015). This combined application could substantially reduce the labor cost but might double the extension cost because of the increased need for government and social publicities. The total costs can be calculated by multiplying the wheat-planting areas, coverage rate (20 % for a pessimistic scenario or 60 % for an optimistic scenario) and a 10-year time horizon (Ma et al. 2008). Thereafter, the cost-effectiveness analysis was performed for the foliar Zn fertilization alone or plus pesticide, according to the handbook of "disability-adjusted life year" and related studies (Stein et al. 2005; Meenakshi et al. 2010; De Steur et al. 2012).

3 Results and discussion

3.1 Health impact of agronomic biofortification of wheat with Zn in China

The estimated health burden values due to human Zn deficiency in the S-W, W-M, and W-R regions are 0.21, 0.79, and 0.38 million "disability-adjusted life years" lost, respectively. These results indicate that the wheat-based regions in central and northern China have been affected by Zn deficiency as the rice-based regions in southern China (Ma et al. 2008; De Steur et al. 2012), although China's economy has rapidly developed for recent 30 years (Stone 2012). This also supports the view that China urgently requires the biofortification of wheat with Zn for an improvement of its living standard (Asare-Marfo et al. 2013).

Like the genetic biofortification (Rosado et al. 2009), the agronomic biofortification of wheat with Zn is also expected to increase the daily Zn intake by infants and children who consume foods derived from Zn-biofortified wheat flour, i.e., such wheat flour with an increased concentration and bioavailability of Zn after the foliar Zn application (Zhang et al. 2012). In the present study, the daily Zn intake is predicted to increase from 4.9-6.0 mg per day without biofortification to 5.2-8.0 mg per day with biofortification, achieving 75 to 100 %of the recommended Zn intake (Table 1). Furthermore, these increases in the daily Zn intake are projected to improve the health of consumers as indicated by the "disability-adjusted life years" saved. Under the pessimistic scenario, 27,990, 96,329, and 33,552 "disability-adjusted life years" lost could be saved in the S-W, W-M and W-R regions, accounting for 13.1, 12.3, and 8.9 % of the current health burden, respectively. Under the optimistic scenario, the saved percentage of the health burden would be increased to 56.6, 55.7, and 32.8 %, respectively (Table 1). These projected reductions in the health burden are comparable with those results from the genetic biofortification of cereals with Zn in India (Stein et al. 2007) or from the genetic multi-biofortification of rice in China (De Steur et al. 2012). Our results thus indicate that the agronomic biofortification of wheat with Zn is a feasible strategy for overcoming human Zn deficiency in regions with wheat-based diets (Ma et al. 2008). Considering their high dependence on wheat as staple food and the health impact of agronomic biofortification (Table 1), the S-W and W-M regions are urgently required for implementing the agronomic biofortification of wheat with Zn (Asare-Marfo et al. 2013).

3.2 Cost-effectiveness analysis for the agronomic biofortification of wheat with Zn

A critical concern regarding the agronomic biofortification of wheat with Zn in the Global South is its economy feasibility (Qaim et al. 2007; Bouis et al. 2011). Our cost-effectiveness analysis shows that a range of US\$ 226 to US\$ 594 is needed to save one "disability-adjusted life year" when the foliar Zn application is sprayed alone. This cost is high because of the required labor (Table 2), which is consistent with the assumption that the agronomic biofortification of wheat with Zn is expensive (Velu et al. 2014; Joy et al. 2015). When a combined foliar application of Zn fertilizer plus pesticide is sprayed, however, the labor cost drops, and only US\$ 41 to US\$ 108 is needed to save one "disability-adjusted life year" (Table 2). Field studies have shown that the Zn concentration in wheat grain is similar whether the Zn is sprayed alone or plus with pesticide (Ram et al. 2015, 2016; Wang et al. 2015). Moreover, the combined application of Zn fertilizer and pesticide is becoming increasingly practical and less expensive under the specialized and integrated management which is compatible with the characteristic of intensive agriculture in China.

An intervention is considered highly cost-effective when the cost per "disability-adjusted life year" saved is less than US\$ 258 according to the World Bank (De Steur et al. 2012). Thus, the combined foliar application of Zn plus pesticide to wheat is highly cost-effective. But it is less cost-effective than the genetic biofortification because the cost for saving one "disabilityadjusted life year" by the genetic biofortification could be less than US\$ 20 due to long-term effects (Stein et al. 2007; Meenakshi et al. 2010; De Steur et al. 2012). Even so, the cost of the agronomic biofortification for overcoming human Zn deficiency in China is competitive with the cost of medical supplementation (US\$ 399), food fortification (US\$ 153), and dietary diversification (US\$ 103) (Ma et al. 2008). Moreover, the foliar application of Zn alone or plus with pesticide has simultaneously increased the wheat yield by a range of 3-7 % in seven countries including China (Zou et al. 2012; Ram et al. 2016). And the residual Zn on the wheat plant and soil surface after foliar application would be ultimately incorporated into soil by straw return and plowing, leading to an increase of Zn in the succeeding crops (Alloway 2008; Solymosi and Bertrand 2012). In addition to increasing the Zn content of wheat seeds, a foliar Zn application can also increase the germination rate of the seeds, the vigor of seedlings, and the final grain yield under Zn-deficient conditions (Yilmaz et al. 1998). As a result, our studies display that the



Table 2Cost-effectivenessanalysis (CEA) of agronomicbiofortification of wheat with Znin three major wheat croppingsystems in China

Parameters	Foliar application of Zn alone			Foliar application of Zn plus pesticide		
	S-W	W-M	W-R	S-W	W-M	W-R
Costs (US\$ ha ⁻¹)						
Zn fertilizer ^a	1.1	1.1	1.1	1.1	1.1	1.1
Agro-equipment ^b	0.72	0.72	0.72	0.72	0.72	0.72
Labor ^c	20.0	20.0	20.0	2.0	2.0	2.0
Social marketing ^d	_	_	_	_	_	-
Extension ^e	0.10	0.10	0.10	0.20	0.20	0.20
Pessimistic scenario						
Coverage rate (%)	20.0	20.0	20.0	20.0	20.0	20.0
Costs (US\$ million) ^d	91.0	510.6	199.4	16.6	93.0	36.3
CEA (US\$ per "disability-adjusted life year" saved)	434.1	530.1	594.3	79.0	96.5	108.2
Optimistic scenario						
Coverage rate (%)	60.0	60.0	60.0	60.0	60.0	60.0
Costs (US\$ million) ^d	273.1	1531.8	598.2	49.7	278.9	108.9
CEA (US\$ per "disability-adjusted life year" saved)	226.4	349.7	482.6	41.2	63.7	87.9

S-W single wheat plantation, W-M wheat-maize rotation, W-R wheat-rice rotation

^a Agriculture-used ZnSO₄·7H₂O was used with a price of US\$ 443 per ton, and the amount of foliar Zn application was according to Zhang et al. 2012

^b Equipments included a motorized sprayer (US\$ 59) and water tank (501, US\$ 5.91). These equipments could be used at least for 90 ha (40 days per year \times 1.5 ha per day \times 3 years \div 2-time spray per year = 90 ha)

^c The averaged labor cost is US\$ 15 per day according to multi-site farmer surveys. One worker can spray 1.5 ha per day, and two sprays are needed. Thus the labor cost was US\$ $15 \div 1.5 \times 2 =$ US\$ 20 per hectare

^d A 10-year time horizon was chosen based on Ma et al. (2008) who studied micronutrient deficiencies in China, while the agronomic biofortification was seen as a short-term strategy (Cakmak 2008)

^e Extension cost was expected to be double due to the need for increased government and social publicity when foliar Zn application is sprayed together with pesticide

agronomic biofortification of wheat through the combined foliar application of Zn fertilizer plus pesticide is a ready-to-use, safe, sustainable, and cost-effective way to overcome human Zn deficiency, particularly in wheat-dominated rural areas.

4 Conclusion

By estimating the cost of the agronomic biofortification of wheat with Zn for human health from extensive field experiments in China and other countries, this study provide a preliminary costeffectiveness analysis by the "disability-adjusted life year" method. The health burden due to human Zn deficiency in the wheatdominated regions of China is substantial. Fortunately, the consumption of products from wheats that have been agronomically biofortified by foliar Zn application could improve the daily Zn intake of infants and, especially, children under 5 years of age. This improvement can thereby reduce the health burden due to human Zn deficiency in regions with wheat-based diets in China. Furthermore, compared to all relevant costs associated with the foliar application of Zn alone, our findings demonstrate that the combined foliar application of Zn fertilizer plus pesticide is a

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highly cost-effective agronomic approach to biofortify wheat with Zn. We therefore conclude that the agronomic biofortification of wheat with Zn through the combined foliar application of Zn plus pesticide is a cost-effective, worthwhile and ready-to-use strategy to fight human Zn deficiency in wheatdominated regions around the world.

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